Interferon Regulatory Factor 2 (IRF 2) Regulates Molecular Pathogenesis of West Nile Virus (WNV) Infection in Brain Cells

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Background: West Nile Virus is a re-emerging disease that affects largely the immuno-compromised, and the patient is often at risk of developing potentially fatal encephalitis. The molecular pathogenesis of WNV infection leading to encephalitis however, has yet to be illustrated. The unveiling of the pathways involved would thus provide insight to the events leading to encephalitis.

Methods: Real-time PCR was used to profile the differential regulation of various interferon regulatory factors (IRF) at 0, 3 and 6 h post-WNV infection. Subsequently, A172 (astrocyte) stable cell-lines having either over-expressed or down-regulated IRF 2 levels were established through lentiviral transduction. Respective cell lines were infected at an MOI of 1 and progeny virus titered to ascertain the consequential effect. Finally, electron microscopy would be performed to image the effect of WNV infection in the astrocytes.

Results: Real-time PCR profiling of IRFs indicated that IRF 2 mRNA level peaked at 3h post-infection. Infection of WNV on IRF2 over-expression A172 cells gave an average virus titer of 2.57×10^6 pfu/ml compared to an average virus titer of 5.00×10^5 pfu/ml in the control cells. On the other hand, infection of WNV on IRF2 down-regulation A172 cells yielded an average virus titer of 5.67×10^5 pfu/ml as compared to an average virus titer of 1.83×10^6 pfu/ml in the control cells. The difference in virus titers in each group was found to be significant using the paired t-test; p-values = 0.0085 and 0.0238 respectively.

Conclusion: Up-regulation of the type I IFN response-attenuator, IRF 2, during WNV infection suggests a likely host-virus interaction. Correlation between IRF 2 levels and WNV titer further exemplifies this possibility. The impact of such a response would be discussed in parallel with images obtained from electron microscopy imaging.

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The Study on Relation of Human Papillomavirus High Risk Types with Bladder Transitional Cell Carcinoma

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Background: Carcinoma of bladder is one of the most common types of cancer in the world. Among different risk factors of bladder carcinoma, the role of genital Human Papillumavirus in TCC was the aim of this study.

Methods and materials: formalin- fixed, paraffin embedded tissue samples of 147 patients with TCC and 39 non-neoplastic cases as a control group were tested for the presence of HPV DNA by nested PCR using the general primer GP5+/GP6+. Genotyping was performed by type specific primers.

Results and conclusion: The positive rates of HPV DNA were 34.7% and 7.6% in case and control groups, respectively and HPV18 was the most common type in association with TCC. There is a meaningful relation between genital HPV infection and bladder carcinoma among Iranian patients. The ratio of male to female was the same in both case and control groups and it was about 6.4. Investigation of age classification showed that the highest number of case group patients aged 51—60 years old.

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Alanine-Scanning Mutagenesis for Revealing the Role of Highly Conserved Regions of Influenza A Virus Neuraminidase

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Background: Neuraminidase (NA), a surface glycoprotein of influenza A virus, is an important molecular target for antiviral drugs. Recent reported NA-inhibition drug resistant cases, such as mutation in H274Y in N1 and R292K and E119G/A/D in N9 and N2, however, has raised concerns about the needs for better understanding NA functional role towards developing a new anti-influenza drug.

Methods: Twenty-eight highly conserved amino acid residues in influenza A viral NA protein were identified through *in silico* analysis based on 2,827 NA sequences deposited in GenBank, NCBI. To understand the role of conserved residues on viral viability, we have introduced series mutations (alanine substitutions) into NA by reverse genetics using A/WSN/33(H1N1) as a backbone.

Results: Seven out of 28 mutants were rescued, indicating that the other 21 positions in NA are essential to viral viability. Among those 21 lethal mutants, 5 were rescued by exogenously adding NA from *C. perfringens*, suggesting that these 5 positions may reside on the NA active site. This assumption was reinforced by structural modeling by SWISS-MODEL. By simulation, we also found 9/21 mutants are located on the side-surface of NA protein. When being substituted, they remarkably reduced the virus survival by losing its biological function, possibly due to the associated structural alteration.

Conclusion: This study identified several amino acid residues important for viral viability. Via structural simulation they are found located at NA active sites or oligomerization sites. We believe the results obtained herein provide valuable information in antiviral drug design based on targeting influenza NA protein.

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